PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

1819

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Applicant's or agent's file reference see form PCT/ISA/220	Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet) **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2005/000874	28.01.2005	30.01.2004

International Patent Classification (IPC) or both national classification and IPC
C07D207/12, A61K31/4015, A61P11/06

Applicant
NOVARTIS AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2005/000874

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2005/000874

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2-11
	No:	Claims	1
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-11
Industrial applicability (IA)	Yes:	Claims	1-11
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

and /or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

see form 210

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

The following documents (D) are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

D1: US-B1-6 605 623 (KO SOO S ET AL) 12 August 2003 (2003-08-12)

D2: WO 03/077907 A (NOVARTIS AG; NOVARTIS PHARMA GMBH; LE GRAND, DARREN, MARK; MCCARTHY, C) 25 September 2003 (2003-09-25)

D3: VARNES, JEFFREY G. ET AL: "Discovery of N-propylurea 3-benzylpiperidines as selective CC chemokine receptor-3 (CCR3) antagonists" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS , 14(7), 1645-1649 CODEN: BMCLE8; ISSN: 0960-894X, 2004, XP002332418

item **V**

1. Novelty (Art. 33(2) PCT)

Document D1 discloses compounds which are modulators of CCR3 (abstract). The generic formula dislcosed on columns 15-16 overlaps with the generic definition of present claim 1 (D1: formula (I), M is absent, Q is CH_2, J and K are CH_2, CHR^5, CHR^6, Z is O, R^1 and R^2 are H, R^3 is ... r =0 (col. 22, l. 34), R^6 is $(CH_2)_rC(O)R^{6b}$ and R^{6b} is phenyl substituted with 0-3 R^{6c}). The overlap is considered novelty destroying for present claim 1. The application thus does not meet the requirements of Art. 33(2) PCT. The subject matter of claims 2-11 is considered novel with respect to D1 (X in claim 2 is O).

2. Inventive step (Art. 33(3) PCT)

2.1. The presently claimed compounds only differ from the specific examples 152-158 on col. 117 and examples 5-7 on col. 177 of D1 only in that the group T cannot be attached to the N-cyclus via a group CH_2. According to the general teaching of D1, however, this linker is not required (see col. 16, definition of R^5 and R^6). The skilled person can thus be expected to provide, starting from the specific examples mentioned, further compounds within the general structure of D1 in order to solve the technical problem of providing alternative CCR3 modulators. The provision of compounds according to present claims 1-4 is thus not considered based on an inventive step within the meaning

of Art. 33(3) PCT.

2.2. Document D2 discloses azetidine compounds as CCR3 receptor antagonists (abstract). The presently claimed compounds differ therefrom in the size of the N-ring (see in particular examples 20-57,66-128,129,130,134-202 of D2). Changing the ring size can be considered obvious for the skilled person who has set himself the task of providing alternative CCR3 receptor modulators because D1 teaches the use of different ring sizes. A combination of the technical teachings of D1 and D2 thus leads to the presently claimed subject-matter, the requirements of Art. 33(3) PCT are thus not met.

2.3. The independent claims 5-11 would not appear to relate to subject-matter which can be considered based on an inventive step as long as the product claims the depend on are not in accordance with the requirements of Art. 33(3) PCT.

3. Industrial applicability (Art. 33(4) PCT)

Can be acknowledged for claims 1-11.

item **VI**

Document D3 was published after the priority date of the present application but before its international filing date. Its content would be considered as forming part of the state of the art if the priority of the present application was found to be invalid.

item **VII**

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1 and D2 is not mentioned in the description, nor are these documents identified therein.